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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

CRANE, L

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 05/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/192,167	Applicant(s) Meade et al.	
	Examiner L. E. Crane	Group Art Unit 1623	

**- THE MAILING DATE of this communication appears on the cover sheet beneath
correspondenc address -**

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE --3-- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be filed after six months from the date of this communication.
- If the prior for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 USC §133).

Status

- ☒ Responsive to communication(s) filed on -11/28/00 (IDS) and 04/19/01 (CPA & amdt B)-.
☐ This action is **FINAL**.
☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claims ---2-11 & 13-15--- are pending in the application. Claim -12- has been cancelled.
Of the above claim(s) ---0--- is/are withdrawn from consideration.
☐ Claims ---0--- is/are allowed.
☒ Claim(s) ---2-11 and 13-15--- are rejected.
☐ Claim(s) ---0--- is/are objected to.
☐ Claim(s) ---0--- are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The proposed drawing correction, filed on -0- is ☐ approved ☐ disapproved.
☐ The drawing(s) filed on -0- is/are objected to by the Examiner.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119(a)-(d)

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119 (a)-(d).
☐ All ☐ Some^o ☐ None of the CERTIFIED copies of the priority documents have been received.
☐ received in Application No. (Series Code/Serial Number) -0-.
☐ received in the national stage application from the International Bureau (PCT Rule 17.2(a)).
* Certified copies not received: -0-.

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). --11-- ☐ Interview Summary, PTO-413
☐ Notice of Reference(s) Cited, PTO-892 ☐ Notice of Informal Patent Application, PTO-152
☐ Notice of Draftsperson's Patent Drawing Review, PTO-948 ☒ Other: -unmailed PTO-1449/892's-.

U.S. Patent Trademark Office

Office Action Summary

PTO-326 (Rev. 04/18/01)
S. N. 09/192,167

Part of Paper No. 15

Copy for ☒ FILE ☐ APPLICANT

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The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1600, Art Unit 1623.

5 Claim 12 has been cancelled, new claim 15 has been added, and claims 5-11 and 13-15 have been amended, and no new claims have been added as per the preliminary amendments filed April 19, 2001. An Information Disclosure Statement (IDS) including references filed November 28, 2000 has also been received and made of record.

10 Claims 2-11 and 13-15 remain in the case.

15 Note to applicant: The pages entitled VERSION WITH MARKINGS TO SHOW CHANGES MADE are incorrectly presented, because the portions of the claims deleted have not been shown within square brackets: e.g, in claim 5 the term replaced [is] has not been shown, and claims wherein no changes have been made (claim 7) are presented as if changes have been made when no changes are evident.

20 Note to applicant (repeated second time): In each of the claims applicant is encouraged to define the new chemical reactants, particularly the newly modified nucleoside reactants and products, with complete chemical structures.

25 Claims 2-11 and 13-14 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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In claim 7 the term "comprising" (first and third occurrences only) is incorrect in the instant claim because said term implies that the chemical structure of the compound being claimed contains additional structural component(s) not defined in the claim.

- 5 Applicant is respectfully requested to substitute narrow language such as -- consisting of -- or the like for the noted term. The same problem reoccurs in claims 2 and 3.

Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

- 10 Applicant argues that "comprising" is proper in all claims directed to all chemical compounds. Examiner respectfully disagrees. When the compounds (starting materials, intermediates and products) are each single molecules as herein, as opposed to a collection of polymeric chains of various lengths and monomer sequences then the
- 15 term "comprising" is incorrect because the metes and bounds of each compound are describable by a single chemical structure and, as herein, there is no good reason not to completely describe, by chemical name or chemical structure, each and every compound within the process. Applicant also argues that "it is the prior art
- 20 that determines whether an open ended term such as "comprising" is appropriate." Examiner respectfully disagrees. Applicant's argument oversimplifies the process of patent application claim examination, a process which relies on multiple parts of the U. S. Code and the Code of Federal Regulations to determine patentability
- 25 and the absence thereof, including the appropriateness of judicially recognized terms. Applicant also argues that the presence of the term "comprising" is justified by the presence in the disclosure of

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lists of compounds which may serve as "electron transfer moieties," "compounds which contain primary amines," and related process details. Examiner respectfully disagrees. As noted in the grounds of rejection functional terms of the kind quoted have meanings which may be read to include a vast array of subject matter not included within the disclosure and are therefore lacking in the degree of precision expected in view of 35 U.S.C. §112, second paragraph.

In claim 7, lines 2-5, the terms "an anhydro-nucleoside", "an electron transport moiety", and "an activated anhydro-nucleoside" are generic terms with many possible structural meanings one, some or all of which may or may not be read into the instant claims in view of the total absence of adequate definition of the metes and bounds intended to accompany said terms. For example, with 2-oxo-pyrimidine nucleosides alone (i.e. uridines and cytidines) there are at least 6 possible different anhydro-forms (2'-O², 3'-O², 5'-O², 2'-C⁶; 3'-C⁶ and 5'-C⁶). It is unclear which of these are intended an which are not by reading the instant claim. Also, the term "electron transport moiety" reads on a copper wire and also reads on a functional group which is capable of gaining or losing electrons, e.g. the bio-oxidant NAD⁺ (gains electrons) and its bio-reductant pair NADH (loses electrons) may be modified with linkers to be substituents at the 2'-position of a 2'-deoxy-2'-amino nucleoside. Clearly, neither of these possibilities were contemplated by applicant and are therefore not properly within the metes and bounds of the instant claim. More carefully drafted claims will insure that these alternatives are excluded from within the metes and bounds of applicant's claim.

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Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

Although applicant's submission at p. 13 of the instant response suggests that claim 7 has been amended, no changes appear to have been made. Applicant argues at p. 5, last paragraph, citing a US patent and a District Court decision to the effect that "there is no requirement that a structure be disclosed in a method claim." Examiner respectfully disagrees. Given the alternative possibilities noted in the rejection of record, and the limited scope of applicant's disclosed embodiments, it appears to examiner that chemical structures in the claim would permit allowable subject matter to be claimed without excessive breadth of scope and in a manner which particularly points out and distinctly claims the subject matter at issue. Later beginning in the middle of page 6 applicant argues that the noted terms are "art recognized terms." Applicant then alleges that the use of such terms "without further definition" is common within the open literature. Examiner reminds applicant that patent claims are subject to rules more stringent than the highly variable editorial policies of the plethora of different publicly available scientific journals.

In claim 7, lines 6-8, the terms "cyclization agent" and "cyclized intermediate" are relatively meaningless unless the details of the chemical reaction being alluded to are provided, thereby rendering this portion of the instant claim lacking in adequately defined metes and bounds.

Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

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In claim 7, lines 6-8, the terms "cyclization agent" and "cyclized intermediate" are relatively meaningless unless the details of the chemical reaction being alluded to are provided, thereby rendering this portion of the instant claim lacking in adequately defined metes and bounds.

Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

Applicant is referred to the comments made in response following the preceding two rejections. Applicant argues the MPEP requires examination using the terms as defined by the disclosure. Examiner respectfully disagrees. It is well established that applicant may be their own lexicographer, but also that terms used may not be redefined at variance with the well established meaning of the term in the art (a term in a claim may not be given a meaning repugnant to the usual meaning of that term, *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947)). Applicant is also reminded that reliance on definitions found in the disclosure is also not without limit, because said definitions must also comport with the standards of 35 U. S. C. §112, second paragraph. The quotation of the disclosure at the top of page 7 of the instant response is as follows:

"By the terms 'electron donor moiety', 'electron acceptor moiety', and 'electron transfer moieties' or grammatical equivalents herein refers to molecules capable of electron transfer under certain conditions."

The noted quotation of the instant disclosure fails to meet the standard of 35 U.S.C. §112, second paragraph, to "particularly point

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out" the subject matter being claimed because

- 1) the definition is entirely functional;
- 2) the definition includes the term "grammatical equivalents," a classification of subject matter not further defined; and
- 5 3) the definition fails to limit the subject matter to any specific compounds.

Applicant then argues, relying on the same type of functional language found in the instant claims, that the functional definitions are acceptable and that the noted terms are "meaningless."

- 10 Examiner respectfully disagrees. The noted terms are plainly not without meaning, but they remain insufficiently definite as found within the noted claim. Applicant's reference to Figures 1 and 2 is noted and applicant is encouraged to use the chemical formulas in these Figures as a basis for chemical structures added to the noted
- 15 claim in order to add the needed degree of precision to the instant claims.

In claim 2, adding a phosphoramidite moiety to a nucleoside is possible, but how such a group is being added in this case remains unclear because of the lack of definiteness found in claims 7 and 2.

- 20 Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

- Applicant's claim language now reads "further comprising adding a phosphoramidite group to the 3'-position of said modified nucleoside," language which at once may be interpreted to imply an
- 25 additional step in the process (no reagent specified therefore incomplete) or simply a different starting material (structure not specified therefore also incomplete). Again applicant is respectfully

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requested to use chemical structures to define the process being claimed, and place all of the subject matter being claimed in the independent claim to begin with rather than relying on a strategy wherein confusion concerning meaning is hard to avoid because of
5 reliance on the term "further comprising" in a dependent claim.

In claim 3, adding a phosphoramidite-derivatized nucleoside to the terminus of a "growing" nucleic acid appears to make reference to the Caruthers process of nucleic acid synthesis, but remains incomplete for failure to specify the structural variables which define
10 the complete chemical structural formula of the "phosphoramidite modified nucleoside."

Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

At page 8, line 8, applicant draws "Examiner's attention to
15 "Figure 3, reaction h) ..." which makes examiner's point admirably; applicant needs to incorporate chemical structures into the claims to properly define the metes and bounds of the claimed subject matter. Applicant then argues that broad claims are acceptable in other cases and therefore should be acceptable here. Examiner
20 respectfully notes first, that the citations are not precisely on point, and therefore are advisory only, and secondly the rejection was based on 35 U.S.C. §112, second paragraph, so the issue of breadth is not appropriately discussed or debated here.

In claim 5, the term "nucleoside comprising a nucleoside analog"
25 is indefinite because applicant has not provided adequate guidance within the instant claim or the instant disclosure to permit the ordinary practitioner to determine which compounds qualify as a

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“nucleoside analog” and which do not (an indefinite metes and bounds problem). In addition the newly added term “comprising” renders the entire term technically inaccurate because the term “nucleoside” does not include the subject matter encompassed by the term
5 “nucleoside analogue” and therefore, the latter included term cannot be fairly defined to be included within the former included term.

Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

10 Applicant argues that the noted term is “art recognized” and therefore infers that the term may be used without concern for its effect on the definiteness of instant claim's metes and bounds. Examiner respectfully disagrees, and suggests that applicant needs to consider filing a CIP wherein the definitions of terms like the one noted are more carefully and completely defined. Applicant's
15 introduction of the term “further comprises” is noted, but for the reasons noted in the reformulated rejection, the amendment creates as many problems as it appears to solve. The marked up version of this amended claim is also incorrectly presented ([is] is missing).

20 In claim 8, the term “electron transfer moiety is a transition metal complex comprising a transition metal and at least one ligand” refers to both compounds and substituents, appearing to equate the two, a clear technical error. Said language also remains entirely functional including a term (“at least one”) which lacks an upper bound, so examiner is unable to know what particular complex or
25 complexes applicant is referring to or how said ligand(s) is/are modified for attachment to the resultant product. This error is further compounded by reliance thereon by dependent claim 9.

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Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

Again applicant is encouraged to use a narrower claim construction wherein the structure of the specific embodiments may
5 be easily deduced as an included species.

In claim 9, the term "wherein said transition metal complex comprises a transition metal selected from the group consisting of ruthenium, rhenium, osmium, platinum, cobalt and iron" is technically
10 incorrect and incomplete because the structures of the "transition metal complex" must include other components than a metal or a metal ion; i.e. the complete structure of the implied ligand substituent. Applicant has therefore incompletely defined either the "transition metal complex" or the "electron transfer moieties" by
15 failing to note in the claim all of the structural features intended to be included.

Applicant's arguments with respect to claim(s) 2-11 and 13-14 have been considered but are moot in view of the new grounds of rejection.

Claim 10 contains nearly all of the same problems defined above
20 for claim 7. The term "a covalently attached polydentate ligand" only hints at the structure of the intended product. Also said term is inconsistent with other terms in dependent claims 13 and 14 including "ferrocene" (not a substituent but a compound which includes an Fe^{+2} ion coordinate-covalently bonded to two
25 cyclopentadienyl anions) and "metallocene" (a name for the genus of organometallic compounds which includes ferrocene). As a

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consequence of these technical errors, claims **13 and 14** both lack proper antecedent basis in claim **10**.

Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

5 Applicant's amendments to claim **10** are noted, but are deemed to have failed to effectively address the instant grounds of rejection. Applicant is referred to the responses following the rejections of claim **7**.

10 In claim **11**, the term "the coordinating atom of said ligand" does not specify and therefore does not include a description of the overall structure of the ligand being claimed and is technically inaccurate (no ligand known to this examiner to be commonly in use relies on a single coordinating "atom"). Applicant appears to err when equating the noted term with the term "an organometallic
15 ligand" as found in claims **13 and 14** because in claims **13 and 14** the exemplification indicated is not merely a ligand, but a complex of a ligand and a metal ion, aka an organometallic complex moiety.

Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

20 Applicant is again encouraged to incorporate as many structural formulas as appropriate to properly define the metes and bounds of the claimed subject matter. Otherwise applicant is respectfully requested to note the responses following previous rejections supra for guidance concerning how to effectively amend the instant noted
25 claims.

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Claims 2-11 and 13-15 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claims 2-11 and 13-15, the chemical reactants are described using generic terms only, thereby encompassing a substantial area of subject matter for which applicant has failed to provide adequate enabling support within the instant disclosure. Specifically terms such as "anhydro-nucleoside" (claim 1), and "nucleoside analog" (claim 5) is directed to a vast array of chemical structures while applicant's specification only discloses a limited number of specific embodiments, leaving the ordinary practitioner the unreasonable burden of determining which claimed embodiments are actually operative and which are not (undue experimentation).

Applicant's arguments filed April 19, 2001 have been fully considered but they are not persuasive.

Applicant has not responded specifically to this rejection but makes reference to responses made to rejections under 35 U.S.C §112, second paragraph. This is non-responsive.

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

"A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been

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obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made."

5 Claims 2-11 and 13-15 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nexstar '102 (PTO-892 ref. L).

10 The instant claims are directed to a process for making labelled nucleosides from anhydro-nucleosides wherein the label is an "electron transfer moiety," for making the phosphoramidites thereof, and for making standard or modified oligonucleotides or polynucleotides therefrom via phosphoramidite coupling.

15 The Nexstar '102 reference discloses processes for making labelled nucleosides from anhydro-nucleosides, for making the phosphoramidites thereof, and for making standard or modified oligonucleotides or polynucleotides therefrom via phosphoramidite coupling including compounds modified by metal-ion-containing coordination complexes (see pp. 9-10 and structure 1 at p. 9). Applicant is referred to pages 17, 21, 23, 26, 3140, 49, 50 and 53, and claim 1, at p. 59, lines 10-11, and claims 5, 20, 22 and 25 wherein the last three claims disclose the nucleoside starting material, disclose the phosphoramidite analogues of the nucleoside, and imply the use of said phosphoramidites to make oligonucleotides incorporating the modified nucleosides by claiming compounds which could be the product of a phosphoramidite oligonucleotide synthesis.

25 Teachings of the prior art which disclose in detail subject matter which reads on the invention as claimed is deemed to render the instant claims lacking in patentable distinction in view of the noted prior art.

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Therefore, the instant claimed process for making labelled nucleosides from anhydro-nucleosides, for making the phosphoramidites thereof, and for making standard or modified oligonucleotides or polynucleotides therefrom via phosphoramidite coupling, would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

Applicant's arguments with respect to claim(s) 2-11 and 13-14 have been considered but are moot in view of the new grounds of rejection.

Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone numbers for the FAX machines operated by Group 1600 are (703) 308-4556 and 703-305-3592 .

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is 703-308-4639 . The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Gary Geist, can be reached at (703)-308-1701.

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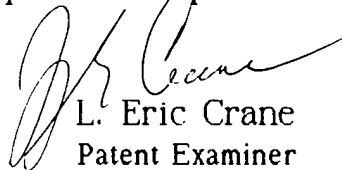
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Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is 703-**308-1235**.

LECrane:lec

5 **05/01/01**


L. Eric Crane
Patent Examiner
Group 1600